

*AMENDMENTS TO THE SPECIFICATION*

Applicants direct entry of the replacement Sequence Listing that is concurrently submitted herewith into the present application.

After paragraph [0001], add the following new section heading and paragraph.

INCORPORATION-BY-REFERENCE OF MATERIAL ELECTRONICALLY  
SUBMITTED

Incorporated by reference in its entirety herein is a computer-readable nucleotide/amino acid sequence listing submitted concurrently herewith and identified as follows: 98,552 bytes ASCII (Text) file named "ReplacementSequenceListing" created November 10, 2011.

Replace paragraph [0014] with:

In one embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of  $M^1X_nTPLGP$  (SEQ ID NO: 214) or  $M^1B_oPZ_mX_nTPLGP$  (SEQ ID NO: 215). In this embodiment, the superscript, 1, denotes the first position of the amino acid sequence of the wild-type G-CSF sequence (SEQ ID NO: 143), the subscripts  $n$ ,  $o$ , and  $m$  are integers selected from 0 to 3, and at least one of X and B is threonine or serine, and when more than one of X and B is threonine or serine, the identity of these moieties is independently selected. Also in this embodiment, Z is selected from glutamate, any uncharged amino acid or dipeptide combination including MQ, GQ, and MV. In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of MVTPLGP (SEQ ID NO: 1), MQTPLGP (SEQ ID NO: 2), MIATPLGP (SEQ ID NO: 3), MATPLGP (SEQ ID NO: 4), MPTQGAMPLGP (SEQ ID NO: 5), MVQTPLGP (SEQ ID NO: 6), MQSTPLGP (SEQ ID NO: 7), MGQTPLGP (SEQ ID NO: 8), MAPTSSSPLGP (SEQ ID NO: 9), and MAPTPLGPA (SEQ ID NO: 10).

Replace paragraph [0015] with:

In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of  $M^1TPXBO_rP$  (SEQ ID NO: 225). In this embodiment the superscript, 1, denotes the first position of the amino acid sequence of the wild-type G-CSF sequence (SEQ

ID NO: 143), and the subscript  $r$  is an integer selected from 0 to 3, and at least one of X, B and O is threonine or serine, and when more than one of X, B and O is threonine or serine, the identity of these moieties is independently selected. In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: MTPTLGP (~~SEQ ID NO: 4~~ SEQ ID NO: 228), MTPTQLGP (SEQ ID NO: 11), MTPTSLGP (SEQ ID NO: 12), MTPTQGP (SEQ ID NO: 13), MTPTSSP (SEQ ID NO: 14), M<sup>1</sup>TPQTP (SEQ ID NO: 15), M<sup>1</sup>TPTGP (SEQ ID NO: 16), M<sup>1</sup>TPLTP (SEQ ID NO: 17), M<sup>1</sup>TPNTGP (SEQ ID NO: 18), MTPLGP (SEQ ID NO: 19), M<sup>1</sup>TPVTP (SEQ ID NO: 20), M<sup>1</sup>TPMVTP (SEQ ID NO: 21), and MT<sup>1</sup>P<sup>2</sup>TQGL<sup>3</sup>G<sup>4</sup>P<sup>5</sup>A<sup>6</sup>S<sup>7</sup> (SEQ ID NO: 22).

Replace paragraph [0016] with:

In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of LGX<sup>53</sup>B<sub>o</sub>LGI (SEQ ID NO: 217), wherein the superscript denotes the position of the amino acid in the wild type G-CSF amino acid sequence, and X is histidine, serine, arginine, glutamic acid or tyrosine, and B is either threonine or serine, and o is an integer from 0 to 3. In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: LGHTLGI (SEQ ID NO: 23), LGSSLGI (SEQ ID NO: 24), LGYSLGI (SEQ ID NO: 25), LGESLGI (SEQ ID NO: 26), and LGSTLGI (SEQ ID NO: 27).

Replace paragraph [0017] with:

In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of P<sup>129</sup>Z<sub>m</sub>J<sub>q</sub>O<sub>r</sub>X<sub>n</sub>PT (SEQ ID NO: 218) wherein the superscript denotes the position of the amino acid in the wild type G-CSF amino acid sequence, and Z, J, O and X are independently selected from threonine or serine, and m, q, r, and n are integers independently selected from 0 to 3. In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: P<sup>129</sup>ATQPT (SEQ ID NO: 28), P<sup>129</sup>TLGPT (SEQ ID NO: 29), P<sup>129</sup>TQGPT (SEQ ID NO: 30), P<sup>129</sup>TSSPT (SEQ ID NO: 31), P<sup>129</sup>TQGAPT (SEQ ID NO: 32), P<sup>129</sup>NTGPT (SEQ ID NO: 33), PALQPTQT (SEQ ID NO: 34), P<sup>129</sup>ALTPT (SEQ ID NO: 35), P<sup>129</sup>MVTPT (SEQ ID NO: 36), P<sup>129</sup>ASSTPT (SEQ ID NO: 37), P<sup>129</sup>TTQP (SEQ ID NO: 38), P<sup>129</sup>NTLP (SEQ

ID NO: 39), P<sup>129</sup>TLQP (SEQ ID NO: 40), MAP<sup>129</sup>ATQPTQGAM (SEQ ID NO: 41), and MP<sup>129</sup>ATTQPTQGAM (SEQ ID NO: 42).

Replace paragraph [0018] with:

In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of PZ<sub>m</sub>U<sub>s</sub>J<sub>q</sub>P<sup>61</sup>O<sub>r</sub>X<sub>n</sub>B<sub>o</sub>C (SEQ ID NO: 219) wherein the superscript denotes the position of the amino acid in the wild type G-CSF amino acid sequence, and at least one of Z, J, O, and U is selected from threonine or serine, and when more than one of Z, J, O and U is threonine or serine, each is independently selected, X and B are any uncharged amino acid or glutamate, and m, s, q, r, n, and o are integers independently selected from 0 to 3. In another embodiment the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: P<sup>61</sup>TSSC (SEQ ID NO: 43), P<sup>61</sup>TSSAC (SEQ ID NO: 44), LGIPTAP<sup>61</sup>LSSC (SEQ ID NO: 45), LGIPTQP<sup>61</sup>LSSC (SEQ ID NO: 46), LGIPTQGP<sup>61</sup>LSSC (SEQ ID NO: 47), LGIPQTP<sup>61</sup>LSSC (SEQ ID NO: 48), LGIPTSP<sup>61</sup>LSSC (SEQ ID NO: 49), LGIPTQP<sup>61</sup>LSSC (SEQ ID NO: 50), LGTPWAP<sup>61</sup>LSSC (SEQ ID NO: 51), LGTPFAP<sup>61</sup>LSSC (SEQ ID NO: 52), P<sup>61</sup>FTP (SEQ ID NO: 53), and SLGAP<sup>58</sup>TAP<sup>61</sup>LSS (SEQ ID NO: 54).

Replace paragraph [0019] with:

In another embodiment the G-CSF polypeptide comprises a mutant peptide sequence with the formula of Ø<sub>a</sub>G<sub>p</sub>J<sub>q</sub>O<sub>r</sub>P<sup>175</sup>X<sub>n</sub>B<sub>o</sub>Z<sub>m</sub>U<sub>s</sub>Ψ<sub>t</sub> (SEQ ID NO: 220) wherein the superscript denotes the position of the amino acid in SEQ ID NO: 143, and at least one of Z, U, O, J, G, Ø, B and X is threonine or serine and when more than one of Z, U, O, J, G, Ø, B and X are threonine or serine, they are independently selected. Ø is optionally R, and G is optionally H. The symbol Ψ represents any uncharged amino acid residue or glutamate, and a, p, q, r, n, o, m, s, and t are integers independently selected from 0 to 3. In another embodiment the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: RHLAQTP<sup>175</sup> (SEQ ID NO: 55), RHLAGQTP<sup>175</sup> (SEQ ID NO: 56), QP<sup>175</sup>TQGAMP (SEQ ID NO: 57), RHLAQTP<sup>175</sup>AM (SEQ ID NO: 58), QP<sup>175</sup>TSSAP (SEQ ID NO: 59), QP<sup>175</sup>TSSAP (SEQ ID NO: 60), QP<sup>175</sup>TQGAMP (SEQ ID NO: 61), QP<sup>175</sup>TQGAM (SEQ ID NO: 62), QP<sup>175</sup>TQGA (SEQ ID NO: 63), QP<sup>175</sup>TVM (SEQ ID NO: 64), QP<sup>175</sup>NTGP (SEQ ID NO: 65), and QP<sup>175</sup>QTLTP (SEQ ID NO: 66).

Replace paragraph [0022] with:

In one embodiment, the hGH polypeptide comprises a mutant peptide sequence with the formula of  $P^{133}JXBOZUK^{140}QTYT$  (SEQ ID NO: 221), wherein superscripts denote the position of the amino acid in (SEQ ID NO: 160); and J is selected from threonine and arginine; X is selected from alanine, glutamine, isoleucine, and threonine; B is selected from glycine, alanine, leucine, valine, asparagine, glutamine, and threonine; O is selected from tyrosine, serine, alanine, and threonine; and Z is selected from isoleucine and methionine; and U is selected from phenylalanine and proline. In another embodiment, the hGH polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: PTTGQIFK (SEQ ID NO: 72), PTTAQIFK (SEQ ID NO: 73), PTTLQIFK (SEQ ID NO: 74), PTTLYVFK (SEQ ID NO: 75), PTTVQIFK (SEQ ID NO: 76), PTTVSIFK (SEQ ID NO: 77), PTTNQIFK (SEQ ID NO: 78), PTTQQIFK (SEQ ID NO: 79), PTATQIFK (SEQ ID NO: 80), PTQGQIFK (SEQ ID NO: 81), PTQGAIFK (SEQ ID NO: 82), PTQGAMFK (SEQ ID NO: 83), PTIGQIFK (SEQ ID NO: 84), PTINQIFK (SEQ ID NO: 85), PTINTIFK (SEQ ID NO: 86), PTILQIFK (SEQ ID NO: 87), PTIVQIFK (SEQ ID NO: 88), PTIQQIFK (SEQ ID NO: 89), PTIAQIFK (SEQ ID NO: 90),  $P^{133}TTTQIFK^{140}QTYT$  (SEQ ID NO: 91), and  $P^{133}TQGAMPK^{140}QTYT$  (SEQ ID NO: 92).

Replace paragraph [0023] with:

In another embodiment, the hGH polypeptide comprises a mutant peptide sequence with the formula of  $P^{133}RTGQIPTQBYS$  (SEQ ID NO: 222) wherein superscripts denote the position of the amino acid in SEQ ID NO: 160; and B is selected from alanine and threonine. In another embodiment, the hGH polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: PRTGQIPTQTYT (SEQ ID NO: 93) and PRTGQIPTQAYS (SEQ ID NO: 94).

Replace paragraph [0024] with:

In another embodiment, the hGH polypeptide comprises a mutant peptide sequence with the formula of  $L^{128}XTBOP^{133}UTG$  (SEQ ID NO: 223) wherein superscripts denote the position of the amino acid in ~~SEQ ID NO: 20~~ SEQ ID NO: 160; and X is selected from glutamic acid, valine and alanine; B is selected from glutamine, glutamic acid, and glycine; O

is selected from serine and threonine; and U is selected from arginine, serine, alanine and leucine. In another embodiment, the hGH polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: LETQSP<sup>133</sup>RTG (SEQ ID NO: 95), LETQSP<sup>133</sup>STG (SEQ ID NO: 96), LETQSP<sup>133</sup>ATG (SEQ ID NO: 97), LETQSP<sup>133</sup>LTG (SEQ ID NO: 98), LETETP<sup>133</sup>R (SEQ ID NO: 99), LETETP<sup>133</sup>A (SEQ ID NO: 100), LVTQSP<sup>133</sup>RTG (SEQ ID NO: 101), LVTETP<sup>133</sup>RTG (SEQ ID NO: 102), LVTETP<sup>133</sup>ATG (SEQ ID NO: 103), and LATGSP<sup>133</sup>RTG (SEQ ID NO: 104).

Replace paragraph [0025] with:

In another embodiment the hGH polypeptide comprises a mutant peptide sequence with the formula of M<sup>1</sup>BPTX<sub>n</sub>Z<sub>m</sub>OPLSRL (SEQ ID NO: 224) wherein the superscript 1, denotes the position of the amino acid in SEQ ID NO: 159; and B is selected from phenylalanine, valine and alanine or a combination thereof; X is selected from glutamate, valine and proline Z is threonine; O is selected from leucine and isoleucine; and when X is proline, Z is threonine; and wherein n and m are integers selected from 0 and 2. In another embodiment, the hGH polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: M<sup>1</sup>FPTE IPLSRL (SEQ ID NO: 105), M<sup>1</sup>FPTV LPLSRL (SEQ ID NO: 106), and M<sup>1</sup>APTPTIPLSRL (SEQ ID NO: 107).

Replace paragraph [0519] with:

In the N-terminal mutants, the N-terminus of a wild-type G-CSF, M<sup>1</sup>TPLGPA (SEQ ID NO: 181), is replaced with either M<sup>1</sup>X<sub>n</sub>TPLGPA (SEQ ID NO: 226) or M<sup>1</sup>B<sub>o</sub>PZ<sub>m</sub>X<sub>n</sub>TPLGPA (SEQ ID NO: 227). Wherein n, o and m are integers ~~selected~~ selected from 0 to 3, and at least one of X, B and O is Thr or Ser. When more than one of X, B and O is Thr or Ser, the identity of these moieties is independently selected. Where they appear, superscripts denote the position of the amino acid in the wild-type starting sequence.

Replace paragraph [0521] with:

In these mutants, the N-terminus of a wild-type GCSF, M<sup>1</sup>TPLGP (SEQ ID NO: 190), is replaced with M<sup>1</sup>TPX<sub>n</sub>B<sub>o</sub>O<sub>r</sub>P (SEQ ID NO: 216). Wherein n, o and r are integers ~~selected~~ selected from 0 to 3, and at least one of X, B and O is Thr or Ser. When more than one of X,

B and O is Thr or Ser, the identity of these moieties is independently selected. Where they appear, superscripts denote the position of the amino acid in the wild-type starting sequence.

Replace paragraph [0523] with:

This mutation is made for the purpose of maintaining G-CSF activity. In these mutants, the amino acid sequence containing H<sup>53</sup>, LGH<sup>53</sup>SLGI (SEQ ID NO: 191) is mutated to ~~LGH<sup>53</sup>B<sub>0</sub>LGI~~ LGX<sup>53</sup>B<sub>0</sub>LGI (SEQ ID NO: 217), where  $[[\Theta]]$  X is H, S, R, E or Y, and B is either Thr or Ser.

Replace paragraph [0525] with:

In this type of mutant, the amino acid sequence encompassing P<sup>129</sup>, P<sup>129</sup>ALQPT (SEQ ID NO: 192), is mutated to P<sup>129</sup>Z<sub>m</sub>J<sub>q</sub>O<sub>r</sub>X<sub>n</sub>PT (SEQ ID NO: 218), wherein Z, J, O and X are independently selected from Thr or Ser, and m, q, r, and n are integers ~~selected~~ selected from 0 to 3.

Replace paragraph [0527] with:

In this type of mutant, the amino acid sequence surrounding P<sup>61</sup>, LGIPWAP<sup>61</sup>LSSC (SEQ ID NO: 213), is replaced with PZ<sub>m</sub>U<sub>s</sub>J<sub>q</sub>P<sup>61</sup>O<sub>r</sub>X<sub>n</sub>B<sub>o</sub>C (SEQ ID NO: 219), wherein m, s, q, r, n, and o are integers ~~selected~~ selected from 0 to 3, and at least one of Z, J, O, X, B and U is selected as either Thr or Ser. When more than one of Z, J, O, X, B and U is Thr or Ser, each is independently selected.

Replace paragraph [0529] with:

In this type of mutant, the amino acid sequence at the C-terminus of a wild-type G-CSF, RHLAQP<sup>175</sup> (SEQ ID NO: 193) is replaced with Ø<sub>a</sub>G<sub>p</sub>J<sub>q</sub>O<sub>r</sub>P<sup>175</sup>X<sub>n</sub>B<sub>o</sub>Z<sub>m</sub>U<sub>s</sub>Ψ<sub>t</sub> (SEQ ID NO: 220), wherein a, p, q, r, n, o, m, s, and t are integers ~~selected~~ selected from 0 to 3, and at least one of Z, U, O, J, G, Ø, B and X is Thr or Ser and when more than one of Z, U, O, J, G, Ø, B and X are Thr or Ser, they are independently selected. Ø is optionally R, and G is optionally H. The symbol Ψ represents any uncharged amino acid residue or E (glutamate).